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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,469	04/20/2001	William D. Huse	P-IX 4692	2981

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EXAMINER

BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 08/12/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/839,469

Applicant(s)

Huse et al

Examiner

Maurie G. Baker, Ph.D.

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 19, 2003
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

DETAILED ACTION

1. The Response filed on May 19, 2003 (Paper No. 10) is acknowledged. No claims were cancelled, added or amended in this response. Therefore, claims 1-9 are pending and under examination.

Status of Rejections and Objections

2. The objection to the specification is withdrawn in view of applicant's amendments thereto. All of the previous rejections are maintained. Response to applicant's arguments are set forth following each rejection.

Maintained Rejections Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a method of determining binding of a "receptor" to one or more "ligands". The claims use generic terminology such as "collective receptor variant population", "binding activity" and "optimal binding affinity". These terms are defined in the instant disclosure but the definitions are very broad.

The language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175).

The specification discloses very limited and mostly prophetic examples of carrying out the claimed method. The claimed receptors and ligands could encompass very different moieties such as peptides, oligonucleotides or other organic molecules. Also, claims 6 and 7 require specific techniques of producing the ligands (recombinant expression in melanophore cells) and claim 9 requires tagging. None of these techniques are adequately described in the instant disclosure.

Thus, the disclosure simply does not provide adequate support to show possession of the claimed invention. The disclosure is neither representative of

the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

Response to Arguments

5. Applicant's arguments filed May 19, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below. Please also see Response to Arguments set forth in paragraphs 14-18 below.

6. Applicant argues that the claims are adequately described and sets forth various citations/definitions from the instant specification concerning the terms discussed in the rejection (see Response, pages 6-9). The examiner acknowledged these definitions in the rejection above but stated that they were *very broad*. The "collective receptor variant population" recited in the claims could encompass a virtually unlimited number of compounds. This is because the instant claims give *no structure* for the receptor itself and no structural information as to the specific "variant". Thus the claims could encompass an infinite number of variations. As also stated above, the examiner pointed out that the specification discloses only very limited and mostly prophetic examples of carrying out the claimed method. This is discussed further below (paragraphs 7-9).

7. Applicant argues that no working examples are necessary (Response, page 8 and elsewhere) and that Example V in the instant specification provides adequate support (see Response, page 8-9). While an example is indeed not required, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art (see below). One of ordinary skill would not necessarily expect to be able to extrapolate the disclosed specific example (i.e. Example V) as far as its applicability to the instant generic claims.

8. With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (cited above) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by “representative examples”) for both enablement and adequate disclosure. A representative number of species means that the species that are adequately described are representative of the entire genus. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation

within the genus. The examiner's position is that a sufficient variety of species have not been described, as the variation within the genus would be extremely large.

9. Also, the examiner deems the art to be unpredictable. The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990).

10. Applicant refers to various teachings from the instant specification to support their argument that the claims are adequately described regarding "binding activity" and "optimal binding affinity" (Response, pages 8-10). First, it is noted that these arguments are not commensurate in scope with the claims. That is, for example, with respect to the arguments regarding Example V, this example is specifically drawn to antibody ligands to BR96 antibody receptor variants and the claims are not limited to such receptors and ligands. Also, although the claims are interpreted in light of the specification, limitations

from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

11. Applicant also refers to various teachings from the instant specification and the prior art to support their argument that the claims are adequately described regarding recombinant expression in melanophore cells and tags (Response, pages 10-11). First, it is noted that these arguments are not commensurate in scope with the claims. That is, for example, with respect to the arguments regarding peptide tags (Response, page 11), the claims are not limited to such tags. With respect to recombinant expression in melanophore cells, applicant discusses transfecting DNA constructs into melanophore cells but the claims are not limited to such receptors. See also paragraph 8 above. Moreover, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

12. Lastly, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). The examiner maintains because of the breadth of the claims, the unpredictability of the art and the lack of adequate

working examples the above standard is not met. Thus, the above rejection of claims 1-9 under 35 U.S.C. 112, first paragraph is deemed to be proper and is maintained.

Maintained Rejections
Claim Rejections - 35 USC § 112

13. Claims 1 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors can include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to a method of determining binding of a “receptor” to one or more “ligands”. No limitations on the specific structure of the ligand or receptor are given and, as such, this could read on a wide variety of structures. The invention is such that

each of the components must be present in operable form for successful practice of the invention. For example, the receptor must bind the ligand and the binding must be able to be detected. Claim 9 specifically requires that the receptor variant is "linked to an identifiable tag". The state of the prior art and the level of predictability in the art: Ligand/receptor binding pairs were well-known in the art at the time of the invention (see art rejections below); however, only limited numbers of such pairs were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of *any* such pair of molecules. The structures of possible variants are sufficiently diverse that one of ordinary skill would not be able to predict their structures with respect to the linking of the receptor variant to an "identifiable tag". The examiner's position is that the art is not predictable to the point that one of ordinary skill could make and use the invention as claimed. Note that the "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. With regard to claim 9, adding tags to the receptors adds to the unpredictability of the claimed method since this type of synthesis requires high efficiency and is further complicated by carryover, cross-reactions, etc., all of

which are acknowledged issues in the art. Each must be dealt with in the optimization of a synthesis scheme. A review article published by Janda discusses these issues (see Proc. Natl. Acad. Sci. 1994; on PTO-1449. See especially page 10782-10785). The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed. The existence of working examples and the quantity of experimentation needed to make or use the invention based on the content of the disclosure: Applicants have provided no specific examples of the claimed method where the receptors are tagged, especially with respect to imparting and decoding the information present in an "identifiable tag" for any receptor. Thus, it is the examiner's position that the instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the claimed invention. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed.

Response to Arguments

14. Applicant's arguments filed May 19, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

15. Applicant argues that the claims are enabled and sets forth various citations/definitions from the instant specification concerning the terms discussed in the rejection (see Response, page 12). However, the terms/methods described by applicant are set forth in only the broadest terminology. As stated in the rejection, no limitations on the specific structure of the ligand or receptor are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the ligand must bind the receptor and the binding must be able to be detected.

16. Applicant argues that the art is not unpredictable and cites prior art in support of such (Response, pages 12-13). The examiner's position is that the art is indeed unpredictable for the reasons set forth in the rejection above. For example, the structures of possible variants are sufficiently diverse that one of ordinary skill would not be able to predict their structures with respect to the linking of the receptor variant to an "identifiable tag". In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. See *In re Fisher*, 57 CCPA 1099, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Additionally, the Board has held on the

issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh* (cited above).

17. Applicant points to various ligand/receptor pairs taught by the prior art. The instant claims are not limited to such pairs or even to any specific pair. The examiner's position is that the instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the claimed invention. Most importantly, *the instant specification fails to identify that structure which is required for the claimed activity.*

In the absence of such guidance, a practitioner of the art would have to resort to a substantial amount of experimental trial and error to produce a "collective receptor variant population" that has the required functional limitations (i.e. "linked to an identifiable tag"). This trial and error would clearly constitute undue experimentation.

18. Applicant also argues that one of ordinary skill would know how to tag the claimed receptors (Response, page 13). The examiner respectfully disagrees as such processes were unpredictable and highly dependent on compound structure (as evidenced by the cited Janda reference). Again, *no structure* for the instant "collective receptor variant population" and no working examples of tagging are provided. See paragraphs 7-8 above with respect to lack of working examples and need for representative examples.

Thus, the above rejection of claims 1-9 under 35 U.S.C. 112, first paragraph is deemed to be proper and is maintained.

Maintained Rejections
Claim Rejections - 35 USC § 112

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites that the receptor variants have “optimal binding activity”. The term “optimal” is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is simply unclear what binding criteria would qualify as “optimal”.

Response to Arguments

21. Applicant’s arguments filed May 19, 2003 have been fully considered but are not found persuasive. The examiner’s rationale is set forth below.

22. Applicant argues that the meaning of the term "optimal" would be apparent to one of ordinary skill and that the instant specification provides sufficient disclosure. The examiner disagrees as the term is relative and the instant specification does not provide a clear and unambiguous definition of what constitutes "optimal binding activity". Note the following from MPEP 2173.02: If the scope of the invention sought to be patented cannot be determined from the language of the claims with a reasonable degree of certainty, a rejection of the claims under 35 U.S.C. 112, second paragraph is appropriate. *In re Wiggins*, 488 F.2d 538, 179 USPQ 421 (CCPA 1973). For these reasons, the above rejection under 35 U.S.C. 112, second paragraph is deemed to be proper and is maintained.

Maintained Rejections
Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Lerner et al (US 5,462,856; on PTO-1449).

Lerner et al disclose a method for identifying a chemical that acts as an agonist for a G-protein coupled cell surface (GPC) receptor (see Abstract). The method uses expression of the receptors in pigment cells, specifically

melanophores (see, for example, column 13, lines 54-67; Example 6 in columns 17-19 and patented claims 9-10). Lerner et al disclose a multiplicity of GPC receptors that are expressed, see, for example, column 14, lines 31-49 and column 15, lines 3-11. The reference clearly teaches “cloning new GPC receptors” (see column 15, lines 17-22; and patented claims 9-10; for example); this reads directly on the claimed “collective receptor variant population”. Lerner et al teaches a variety of bioassays that can be used to screen the GPC receptors for binding to ligands (see Examples 1-5 in columns 15-17); this reads directly on the “contacting” and “detecting” steps of the claimed method. The reference also discloses a procedure for isolating a clone for a GPC receptor via a fractionation procedure (see column 18, line 65 – column 19, line 11). Specifically disclosed is a procedure where colonies are tested, then can be subdivided into smaller pools (such as 10 sets of 1,000 colonies each from a pool of 10,000) based on positive results where each sub-set is retested until a single clone is identified. This reads directly on the “dividing, contacting and detecting” steps of instant claims 2, 3 and 8 and the identification steps of instant claims 4 and 5.

Response to Arguments

25. Applicant's arguments filed May 19, 2003 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

26. Applicant argues that Lerner et al does not teach a “collective receptor variant population” stating that “the subject specification teaches the use of a collective receptor variant population and not random cDNA libraries” (Response, page 16). However, there is nothing in the instant claims or specification that indicates that random cDNA libraries would be excluded from a “collective receptor variant population”. Also, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, importantly, the disclosure of random cDNA libraries in Lerner et al is not the only disclosure of expression of GPC receptors. As pointed out in the rejection, there are many portions of Lerner et al that disclose expression of a multiplicity of receptors. See portion of rejection cited below:

The method uses expression of the receptors in pigment cells, specifically melanophores (see, for example, column 13, lines 54-67; Example 6 in columns 17-19 and patented claims 9-10). Lerner et al disclose a multiplicity of GPC receptors that are expressed, see, for example, column 14, lines 31-49 and column 15, lines 3-11. The reference clearly teaches “cloning new GPC receptors” (see column 15, lines 17-22; and patented claims 9-10; for example); this reads directly on the claimed “collective receptor variant population”.

For these reasons, the above rejection under 35 U.S.C. 102(b) is deemed to be proper and is maintained.

Status of Claims/Conclusion

27. No claims are allowed.

28. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding

should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
August 10, 2003



MAURIE GARCIA BAKER PH.D.
PRIMARY EXAMINER